

U.S. Patent Application Serial No. **10/730,258**
Amendment filed April 17, 2006
Reply to OA dated November 15, 2005

REMARKS

Claims 1-6 are pending in this application. Claim 6 is canceled without prejudice or disclaimer, and claims 1 and 2 are amended herein. Upon entry of this amendment, claims 1-5 will be pending. Entry of this amendment and reconsideration of the rejections are respectfully requested.

No new matter has been introduced by this Amendment. Support for the amendments to the claims is discussed below.

Claims 2-4 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. (Office action paragraph no. 2)

The objection to claims 2-4 is respectfully traversed. Applicant's remarks below address the rejections of base claim 1.

Claims 1-6 are rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. (Office action paragraph no. 3)

The rejection of pending claims 1-5 is respectfully traversed.

The Examiner states that the step of recovering the sporangia from the culture medium has been omitted. However, Applicant first of all notes that this does not amount to a "gap between the steps", since **only one step** is recited in claim 1.

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Moreover, there is no apparent reason why “recovering the sporangia” is in any way essential to practicing the claimed invention. Recovery is discussed in paragraph [0029] of the specification, but it is apparent in this paragraph that the microbial cells containing the sporangia are present in the medium. Therefore, the culturing step recited in claim 1 has produced sporangia, consistent with the preamble of the claim. Applicant submits that nothing in the preamble of claim 1 or claim 5 requires that the sporangia be isolated from the medium.

Reconsideration of the rejection is respectfully requested.

Claims 1 and 5 are rejected under 35 U.S.C. §102(b) as being anticipated by Haynes et al. (Sporogenicity of yeast autolyzates casein hydrolyzates for *Bacillus popilliae* in liquid cultures, *Journal of Invertebrate Pathology*, 1973; 22: 377-81). (Office action paragraph no. 4)

Reconsideration of the rejection is respectfully requested in view of the amendments to the claims. The amendments to claims 1 and 2 clarify that the recited “glutamic acid” is “free glutamic acid,” that is, not a glutamic acid residue conjugated to other amino acids in a peptide. This amendment is fully supported by the specification, for example on page 9, last line, to page 10, line 8, where it is described that glutamic acid or salts thereof (i.e., free glutamic acid) are used in the medium to achieve the desired glutamic acid concentration.

The Examiner cites Haynes et al. on page 377, table 1, and page 381, as disclosing a medium for *B. popilliae* “containing glutamic acid by weight of 18-21g/16g nitrogen”. The Examiner appears

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to be referring to Table 2 on page 379, which discloses the amino acid composition of four lots of yeast extracts used in the media, and their effects on sporogenicity.

Haynes generally reports that spores "will form in liquid, shaken J-medium cultures containing activated carbon and suitable lots of yeast autolyzate", but that "reproducible yields in a range of 10^6 to 10^7 will form only if a suitable lot of casein hydrolyzate is also present" (page 381, column 1, third paragraph). The reference indicates that two lots of Amber products and one Bacto Yeast extract were sporogenic. Table 2 on page 379 reports that two lots of yeast autolyzate, no. 461591 and no. 467969, were sporogenic, and gives the analysis of these lots. The Table lists these lots as having 21.0 and 18.1 g Grams/16g nitrogen, respectively, and also lists these as having 99.8 and 106.7 mg N/g (dry basis).

However, Haynes neither teaches nor even remotely suggests that **free** glutamic acid has an enhancing effect on sporangia formation. Moreover, the reference does not discuss free glutamic acid nor the addition of free glutamic acid into the medium. Therefore, the only issue in the rejection is whether Haynes' medium inherently meets the free glutamic acid limitation of claim 1. Applicant submits that Haynes' medium does **not** meet this limitation.

Haynes discloses the result of amino acid composition analysis of yeast extracts used in the media in Tables 2 and 5. However, hydrolyzed yeast extracts are not simply a mixture of free amino acids, and Tables 2 and 5 have no information as to amount of free glutamic acid and the ratio of free/conjugated glutamic acids. Accordingly, the amount of free glutamic acid **cannot be calculated**

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directly from the disclosure of Haynes. There is no basis for an inherency rejection in the data in the Haynes reference.

Applicant has therefore attempted to estimate the amount of free glutamic acid in Bacto yeast extract and Bacto Tryptone. This estimate is based on data in the *BD (Becton Dickinson) Biopharmaceutical Production Bionutrient Technical Manual*, second edition, (“BD Manual”) attached to this Amendment. In this regard, Applicant notes page 5 of this reference, discussing the general production of hydrolysates to make peptones. Applicant notes that “The resulting material from a proteolytic digestion is a mixture of amino acids and polypeptides of varying lengths” (BD Manual, page 5, 4th paragraph.)

The estimation results are shown below. In the calculation, Applicant has assumed that amount of each amino acid in Haynes is total amount of each amino acid, that is, the sum of the free and conjugated amino acids.

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Haynes Table 2

	Mw	N	Bacto yeast extract	
			Sporogenic	
			461591	487969
Grams/16g nitrogen				
Lys	146.19	2	13.3	12.0
His	155.16	3	1.1	1.7
Arg	174.2	4	2.8	4.4
Asp	133.1	1	10.5	10.8
Thr	119.12	1	5.0	4.9
Ser	105.09	1	5.1	5.3
Glu	147.13	1	21.0	18.1
Pro	115.13	1	2.5	2.7
Gly	75.07	1	4.9	4.7
Ala	89.09	1	8.5	7.2
Cys	121.16	1		
Val	117.15	1	7.0	7.0
Met	149.21	1	1.3	1.5
Ile	131.18	1	4.9	4.9
Leu	131.18	1	6.7	6.9
Tyr	181.19	1	0.7	0.8
Phe	165.19	1	2.7	2.8
mg N/g			99.8	106.7

Estimated amounts in Yeast Ext.

	Bacto yeast extract	
	Sporogenic	
	461591	487969
% (Grams/100g YE)		
Lys	8.30	8.00
His	0.69	1.13
Arg	1.75	2.93
Asp	6.55	7.20
Thr	3.12	3.27
Ser	3.18	3.53
Glu	<u>13.10</u>	<u>12.07</u>
Pro	1.56	1.80
Gly	3.06	3.13
Ala	5.30	4.80
Cys		
Val	4.37	4.67
Met	0.81	1.00
Ile	3.06	3.27
Leu	4.18	4.80
Tyr	0.44	0.53
Phe	1.68	1.87
Total	61.13	63.82

Haynes Table 5

	Mw	N	Bacto Tryptone	
			Sporogenic	
			455854	Grams/16g nitrogen
Grams/16g nitrogen				
Lys	146.19	2	12.4	
His	155.16	3	2.3	
Arg	174.2	4	3.4	
Asp	133.1	1	9.3	
Thr	119.12	1	5.3	
Ser	105.09	1	6.6	
Glu	147.13	1	33.9	
Pro	115.13	1	18.7	
Gly	75.07	1	2.5	
Ala	89.09	1	4.0	
Cys	121.16	1		
Val	117.15	1	8.7	
Met	149.21	1	2.2	
Ile	131.18	1	5.9	
Leu	131.18	1	10.8	
Tyr	181.19	1	5.3	
Phe	165.19	1	3.5	
mg N/g			124.5	

Estimated amounts in Tryptone

	Bacto Tryptone	
	Sporogenic	
	455854	Grams/100g Tryptone
% (Grams/100g Tryptone)		
Lys	9.65	
His	1.79	
Arg	2.65	
Asp	7.24	
Thr	4.12	
Ser	5.14	
Glu	<u>26.38</u>	
Pro	14.55	
Gly	1.95	
Ala	3.11	
Cys		
Val	6.77	
Met	1.71	
Ile	4.59	
Leu	8.40	
Tyr	4.12	
Phe	2.72	
Total		104.89

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For Haynes' combination of yeast extract (461591) and Tryptone (455854), then the amount of free glutamic acid is:

$$13.1 \times 6.6 / 9.4 \times 0.015 + 26.38 \times 1.4 / 15.1 \times 0.005 = 0.150 (\%).$$

For Haynes' combination of yeast extract (467969) and Tryptone (455854), then the amount of free glutamic acid is:

$$12.07 \times 6.6 / 9.4 \times 0.015 + 26.38 \times 1.4 / 15.1 \times 0.005 = 0.139 (\%).$$

Therefore, the medium used in Haynes contains less free glutamic acid than recited in claim 1.

With regard to claim 5, Applicant notes that the *B. popilliae* used in making the control agent of claim 5 are grown in a different medium than those of Haynes, and the present specification has pointed out that the sporangia production in the present invention is clearly different than that in the prior art. The sporangia of claim 5, produced in the process of claim 1, would not be expected to be identical to those of Haynes.

Reconsideration of the rejection is respectfully requested.

Claim 6 is rejected under 35 U.S.C. §103(a) as being obvious over Haynes et al. as applied to claims 1 and 5 above, and further in view of Fujiie et al. (JP 411332556A, abstract only). (Office action paragraph no. 5)

The rejection is moot in view of the cancellation of claim 6 without prejudice or disclaimer.

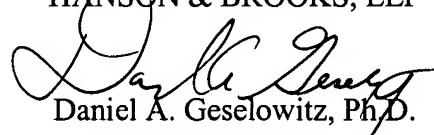
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If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact the applicant's undersigned agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, the applicant respectfully petitions for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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PATENT TRADEMARK OFFICE

Enclosure: Petition for Extension of Time

BD Biopharmaceutical Production Bionutrient Technical Manual, second edition,
(March 2004), obtained from
<http://www.bd.com/ds/technicalCenter/misc/bionutrientmanual.pdf>

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